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Effects of serum biochemical parameters on the prevalence of colon polyps

Colon polyps

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Abstract
Aim: Early detection of colorectal polyps is important to prevent malignant transformation. The levels of several metallic and hematologic parameters may be indicators of these polyps. The objective of this study was to investigate whether iron levels may indicate the presence of colorectal polyps.
Material and Methods: A total of 897 patients who underwent routine biochemical analysis and colonoscopy were retrospectively evaluated. Patients were grouped as polyp (-) and polyp (+) and further divided into two groups as those with neoplastic polyps and the patients with non-neoplastic polyps. The levels of iron, ferritin, hemoglobin, glucose, cholesterol, triglycerides and vitamin D were compared between the groups.
Results: Males accounted for 60.5% of all patients, and 39.5% were females. The mean age of the patients was found as 43.3±11.9 years. The mean iron (p=0.023), ferritin (p=0.002), cholesterol (p=0.008) and triglycerides (p=0.005) levels were significantly higher in patients with polyps compared to those without polyps. The mean iron (p=0.001), ferritin (p<0.001), hemoglobin (p<0.001) and triglyceride (p=0.007) levels were higher in the males compared to the females. The mean iron (p<0.001), ferritin (p<0.001) and cholesterol (p=0.020) levels were significantly higher in patients with neoplastic polyps compared to those with non-neoplastic polyps.
Discussion: Iron levels were elevated in individuals with colorectal polyps and further elevated in patients with neoplastic polyps. Determination of cut-off values of iron and other parameters in predicting colorectal polyps will enable early detection of colorectal polyps and proper intervention.

Keywords
Colorectal polyps; Neoplastic; Non-neoplastic; Iron; Ferritin; Hemoglobin

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Introduction

Colorectal cancer (CRC) is the second most common cancer in women and the third most common cancer in men worldwide [1]. The incidence and the rate of mortality from CRC are increasing all over the world due to several reasons, including urbanization, sedentary life, smoking, excessive alcohol consumption, changed dietary habits and obesity. The pathogenesis of CRC has been well-defined and colorectal polyps play a major role in the etiology of CRC [2]. The association between colorectal polyps and CRC has been reported in epidemiological, clinical and molecular research [3].

Colorectal polyps can be defined as visible protrusions over the surrounding large intestine mucosa. They present as isolated, multiple or diffuse lesions. Colorectal polyps are histologically classified as neoplastic (adenomatous) and non-neoplastic. CRC mainly develops from adenomatous polyps through a process known as adenoma-to-carcinoma sequence [4]. Non-neoplastic polyps do not have malignant potential. Although all adenomatous polyps have malignant potential when detected early enough, most are benign. For polyps that develop into CRC, the time until the development of CRC is accepted as >10 years [5]. This gives enough time to clinicians to perform interventional strategies in order to prevent the transformation of the polyp into cancer [5]. Therefore, it is of paramount importance to start colonoscopy scans to detect colorectal polyps timely. It has been proven that early detection and resection the map of these polyps prevent mortality due to CRC [6].

In general, a routinely ordered blood test sometimes can give abnormal values in certain parameters. It is important to study blood parameters that can be associated with polyps. Screening of these abnormal parameters may help identify populations at high risk for colorectal polyps [7].

Determination of the association between blood parameters and the presence of colorectal polyps may be helpful in the timely intervention to and management of these polyps. However, publications on this issue are limited except for a few studies that have directly investigated the relationship between blood parameters levels and the presence of colorectal polyps [8, 9].

It is known that some metals are involved in the process of polyp formation [10]. Iron is one of the metals found abundantly in the colon. The number of studies in the literature demonstrating the relationship between iron levels and the presence of colorectal polyps is limited. Therefore, the objective of this study was to investigate the relationship between serum iron concentrations and colon polyps, and specifically, neoplastic polyps.

Material and Methods

Patients who presented to our hospital with gastrointestinal complaints and underwent colonoscopy between January 2018 and December 2019 were retrospectively evaluated. Data of the patients were obtained from the information processing system of the hospital. Patients who underwent metabolic panel test and colonoscopy were included in the study. Patients with a history of colorectal surgery, those with a personal or family history of colonic diseases including CRC and inflammatory bowel disease, patients with active infectious disease, rheumatic disease, those who were regularly using vitamin and/or mineral supplements and patients with an elevated CRP level were excluded from the study. In addition, patients with missing data were also excluded. Patients' demographic data such as age and gender, presence of polyps, type of polyps (neoplastic or non-neoplastic), serum levels of iron, ferritin, glycated hemoglobin (HbA1C), blood glucose, cholesterol, triglycerides, and vitamin D were recorded and analyzed.

For the metabolic panel test and serum biochemical analysis, after one-night fasting, blood samples were collected from all patients. Colonoscopy procedures were performed by an experienced endoscopist after bowel preparation with self-administration of 2-4 L of polyethylene glycol solution before the colonoscopy. The sufficiency of bowel preparation was assessed by the endoscopist based on the Boston Bowel Preparation Scale. The samples of all resected polyps were sent to the pathology laboratory for biopsy. Patients were divided into two groups as the patients with and without colon polyps. The patients with polyps were further divided into two groups as those with non-neoplastic polyps and the patients with neoplastic polyps that have malignancy potential. The obtained biochemical parameters were compared between these groups.

Ethics Considerations

Before the beginning of the study, ethics approval was obtained from the local ethics committee of our hospital (Decision No: 71522473/050.01104/404; Date:10/07/2020). The study was conducted in accordance with the ethical guidelines of the Declaration of Helsinki.

Statistical Analysis

The data obtained in this study were statistically analyzed utilizing SPSS 23.0 software for Windows (SPSS Inc., Chicago, IL, USA). The normality of the data was evaluated with the Kolmogorov-Smirnov test. Non-normally distributed variables were compared between two groups using the Mann-Whitney U test. Numerical variables were expressed as mean ± standard deviation, median, minimum and maximum descriptive statistics, while categorical variables are given as frequency (n) and percentage (%). The p-values <0.05 were considered statistically significant.

Results

A total of 897 patients who underwent a colonoscopy procedure in our gastroenterology clinic due to various indications between January 2018 and December 2019 were included in this study. Among all patients, 543 (60.5%) were male. The mean age of the patients was 43.3±11.9 years.

Laboratory parameters were compared between the patients with polyps and those without polyps detected during the colonoscopy procedure. Accordingly, the mean iron level was found as 84.8±37.8 mg/dL (range: 5-256) in the polyp (+) and 71.2+30.8 mg/dL in the polyp (-) group. The mean iron level was statistically significantly higher in the polyp (+) group. In addition, the mean levels of ferritin, cholesterol and triglycerides were also statistically significantly higher in the polyp (+) group compared to the polyp (-) group. Whereas, the levels of HbA1C, glucose and vitamin D did not show a significant difference between the two groups. The comparison of the laboratory parameters between the two groups is given in Table 1.

Table 1. Comparison of the laboratory parameters between the patients with and without polyps

Parameter	POLYPS (-)				POLYPS (+)				p*
	mean	SD	median	min-max	mean	SD	median	min-max	
Iron (mg/dL)	71.2	30.8	73	12-137	84.8	37.8	84.5	5-256	0.023
Ferritin (ng/mL)	51.3	48.4	34.8	5.3-320	79.9	70.1	63.9	4.1-460	0.002
Hemoglobin (g/dL)	5.7	0.6	5.7	4.8-7.4	5.9	0.8	5.7	4.4-9.8	0.366
Glucose (mg/dL)	97.5	16.2	96	79-180	102	32.2	97	71-400	0.338
Cholesterol (mg/dL)	189.2	47.5	190.5	108-356	207.9	52.7	200	24-400	0.008
Triglycerides (mg/dL)	116.6	71.4	100	34-553	142.1	78.7	118	43-558	0.005
Vitamin D (ng/mL)	20.2	70.2	20	5.9-40.1	21.7	16.7	19	5-143	0.634

* Mann-Whitney U test; SD: standard deviation

Table 2. Comparison of the laboratory parameters between male and female patients

Parameter	MALE				FEMALE				p*
	mean	SD	median	min-max	mean	SD	median	min-max	
Iron (mg/dL)	86.5	32.5	88	5-181	71.3	39	68	12-256	0.001
Ferritin (ng/mL)	93.1	72	85.9	7-460	37.9	32.5	25.5	4.1-141	<0.001
Hemoglobin (g/dL)	14.8	1.2	14.9	10.1-17.4	12.7	1.2	12.8	7.8-15	<0.001
Glucose (mg/dL)	98.8	16.6	96	71-184	102.9	38.6	97.3	78-400	0.859
Cholesterol (mg/dL)	201.8	49.2	200	24-321	201.2	55.4	200	100-400	0.589
Triglycerides (mg/dL)	144.9	86.8	119	34-558	116.9	56.8	100	43-296	0.007
Vitamin D (ng/mL)	20.8	11.5	20	5-72	21.9	17.6	19.1	5.9-143	0.969

* Mann-Whitney U test; SD: standard deviation

Table 3. Comparison of iron, ferritin and cholesterol levels between the patients with neoplastic and non-neoplastic polyps

Parameter	NEOPLASTIC POLYPS				NON-NEOPLASTIC POLYPS				p*
	mean	SD	median	min-max	mean	SD	median	min-max	
Iron (mg/dL)	96.5	38.4	100	20-256	74.6	33.6	73	5-181	<0.001
Ferritin (ng/mL)	97.9	83.2	90	5.6-460	60.8	54.6	40	4.1-320	<0.001
Cholesterol (mg/dL)	212.4	52.1	212	24-321	198	51.2	200	100-400	0.020

* Mann -Whitney U test; SD: standard deviation

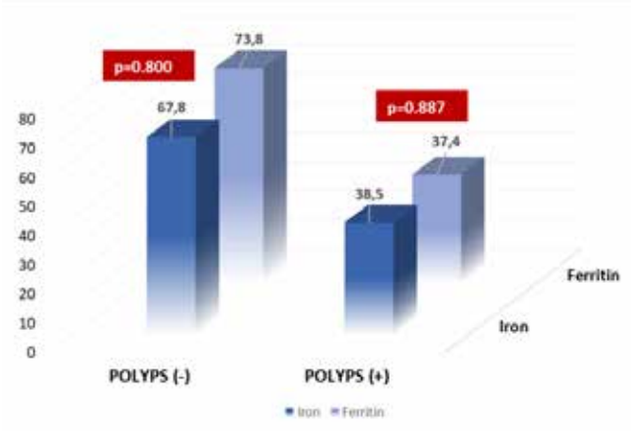

Figure 1. Iron and ferritin levels of the female patients with and without colon polyps

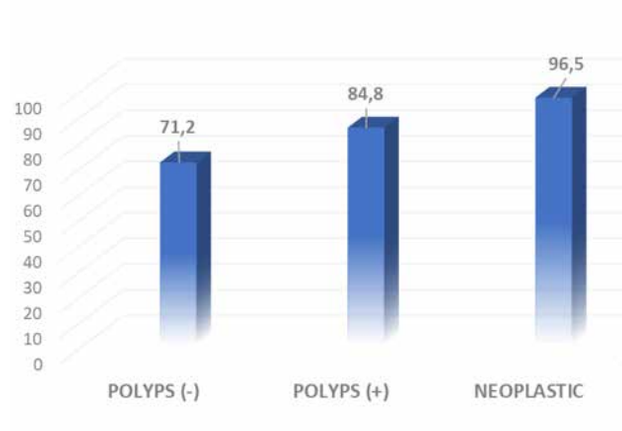

Figure 2. Comparison of mean iron levels between patients with and without colon polyps and those with neoplastic polyps.

The laboratory parameters included in the study were compared between male and female patients. The mean iron value was 86,5+32,5 (range: 5-181) for males and 71,3+39 (range: 12-256) for females. The difference between male and female patients in terms of iron levels was statistically significant (p=0.001). In addition, mean levels of ferritin, hemoglobin, and triglycerides were also significantly higher in male patients. Comparison of the laboratory parameters between male and female patients is shown in Table 2.

The mean iron and ferritin levels were also compared between the female patients with and without polyps. There was no statistically significant difference between them (Figure 1).

The patients with polyps were further divided into two groups according to the classes of the polyps as neoplastic and non-

neoplastic. The laboratory parameters were compared between these two new patient groups. Accordingly, the mean iron, ferritin and cholesterol levels were statistically significantly higher in the neoplastic group compared to the non-neoplastic group. Comparison of these three significant parameters between the two groups is given in Table 3.

Lastly, Figure 2 shows the mean iron levels in polyps (-), polyps (+) patients and those with neoplastic polyps.

Discussion

Metabolic abnormalities are often encountered in individuals with colorectal polyps [7]. Providing insight into the role of essential and non-essential elements involved in the development of polyps is of importance for better understanding of the transformation of colonic polyps into CRC. This can encourage researchers to focus on the elements involved in neoplastic polyps and provide an opportunity for more efficient management of CRC. Unfortunately, so far studies in the literature have focused on metal contents in colorectal cancer [11] and only reported rare data on metal contents of precancerous lesions, namely polyps.

Studies have suggested that high levels of iron increased the risk of CRC in humans through the formation of OH radicals and suppression of cellular immune functions [10]. Another proposed mechanism is that iron-induced oxidative stress and resultant antioxidant depletion, thus oxidant/antioxidant balance promotes carcinogenesis [12]. Iron can accelerate oxidative damage in macromolecules, causing both inflammatory and neoplastic disorders. The concentration of iron is high in the colon, suggesting that this may be associated with the formation of polyps. Iron is involved in the biological function in both normal and cancerous tissue. Ferritin is a major iron storage protein, and its serum levels are associated with body iron stores [13].

In our study, we examined whether iron levels change in polyps, and specifically neoplastic polyps. We found significantly higher iron and ferritin levels in the patients with polyps compared to those without. This result suggests that the level of iron that can be readily obtained as a laboratory parameter, may be an indicator of the presence of colorectal polyps. In a special article, Nelson reported the presence of an association between body iron stores and the development of precancerous lesions in the colon, namely colorectal polyps [14]. Alimonti et al. showed that polyp tissues had a higher level of iron compared to the healthy tissues [10]. Lorenzi et al. found a correlation between high serum ferritin levels and biological events that are closely related to colorectal tumors, such as the growth and proliferation of tumor cells [13]. In our study, iron and ferritin levels were also statistically significantly higher in patients with neoplastic polyps compared to the patients with non-neoplastic polyps. Kucharzewski et al. also reported higher iron levels in colorectal cancer than in polyps [15]. As clearly found in our study (Figure 2), iron levels showed an increase from normal to polyp tissues and then to neoplastic polyp tissues, suggesting that iron may play a role in the adenoma-to-carcinoma sequence of CRC. A cut-off value of iron level can be found with further studies to distinguish neoplastic polyps from non-neoplastic ones.

Hemoglobin, an iron-containing metalloprotein has been shown to be higher in patients with colorectal polyps [16]. In addition, some studies have shown elevated hemoglobin levels in metabolic diseases that are known to be associated with colorectal polyps, such as metabolic syndrome and non-alcoholic fatty liver [8, 17, 18]. In our study, although there was no significant difference between patients with and without colorectal polyps in terms of hemoglobin levels, these levels were significantly higher in patients with neoplastic polyps compared to those with non-neoplastic polyps. This finding may indicate that hemoglobin is involved more in malignant transformation of the colorectal polyp. Similarly, Kim et al. reported that elevated hemoglobin levels were useful in predicting the presence of adenomatous polyps [19].

In the present study, the levels of several metabolic and hematologic elements/parameters were also investigated in colorectal polyps. In addition to iron and ferritin, cholesterol and triglyceride levels were significantly higher in the patients with polyps, while glucose and vitamin D levels did not show statistical significance. Furthermore, cholesterol levels were also significantly higher in patients with neoplastic polyps compared to those with non-neoplastic polyps. The mean levels of iron, ferritin, hemoglobin, and triglycerides were also significantly higher in male patients. This might be caused by the higher overall incidence of colorectal polyps in men compared to women [20]. Due to the abundance of metallic and hematologic parameters that can play a role in the development of the polyp, studies have investigated a wide spectrum of parameters. A systematic review or a meta-analysis to compile the literature on this issue can be of benefit.

In a study by Yang et al., a weak correlation was found between lipids including vitamin D, and the presence of colorectal polyps [21]. Sun et al. studied serum albumin levels and found lower values in patients with colorectal polyps [22]. Magnesium has been shown to exert protective effects against the risk of adenomatous polyps [23, 24]. Alimonti et al. found increased levels of selenium and decreased values of copper and mercury in polyp tissues, while zinc and manganese levels remained unchanged [10]. These metabolic and hematologic parameters can readily be obtained with routine blood analysis, and determination of the association between some of these elements and colorectal polyps can enable developing risk stratification systems to be used in the early detection of colorectal polyps.

Study Limitations

The retrospective and single-center nature of this study may be considered the main limitation. However, the major objective of this study was to investigate the relationship between iron levels and polyps. The number of patients was satisfying for a study of such structure. Finally, given the scarcity of studies in the literature on this issue,we think that our results will be encouraging for future detailed research on metal contents of colorectal polyps.

Conclusions

The results of this study indicate that iron levels were elevated in individuals with colorectal polyps and further elevated in patients with neoplastic polyps. This should prompt clinicians to evaluate iron levels among the other metabolic and hematologic

laboratory parameters in patients suspected to have colorectal polyps. On the other hand, the determination of cut-off values of iron and other parameters in predicting colorectal polyps will be helpful in the development of new risk scoring systems, facilitating early detection of colorectal polyps. Further comprehensive studies are needed in order to enlighten the role of iron in the development of colorectal polyps and to support the findings of this study.

Scientific Responsibility Statement
The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and human rights statement
All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. No animal or human studies were carried out by the authors for this article.

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Conflict of interest
None of the authors received any type of financial support that could be considered potential conflict of interest regarding the manuscript or its submission.

References
1. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2018;68(6):394-424.
2. Aran V, Victorino AP, Thuler LC, Ferreira CG. Colorectal Cancer: Epidemiology, Disease Mechanisms and Interventions to Reduce Onset and Mortality. Clin Colorectal Cancer. 2016 Sep;15(3):195-203.
3. Aran V, Victorino AP, Thuler LC, Ferreira CG. Colorectal Cancer: Epidemiology, Disease Mechanisms and Interventions to Reduce Onset and Mortality. Clin Colorectal Cancer. 2016;15(3):195-203.
4. Bertelson NL, Kalkbrenner KA, Merchea A, Dozois EJ, Landmann RG, De Petris G, et al. Colectomy for endoscopically unresectable polyps: how often is it cancer? Dis Colon Rectum. 2012;55(11):1111-6.
5. Øines M, Helsingen LM, Bretthauer M, Emilsson L. Epidemiology and risk factors of colorectal polyps. Best Pract Res Clin Gastroenterol. 2017;31(4):419-24.
6. Zauber AG, Winawer SJ, O'Brien MJ, Lansdorp-Vogelaar I, van Ballegooijen M, Hankey BF, et al. Colonoscopic polypectomy and long-term prevention of colorectal-cancer deaths. N Engl J Med. 2012;366(8):687-96.
7. Kinar Y, Akiva P, Choman E, Kariv R, Shalev V, Levin B, et al. Performance analysis of a machine learning flagging system used to identify a group of individuals at a high risk for colorectal cancer. PLoS One. 2017;12(2):e0171759.
8. Chung GE, Yim JY, Kim D, Kwak MS, Yang JI, Chung SJ, et al. Associations between hemoglobin concentrations and the development of incidental metabolic syndrome or nonalcoholic fatty liver disease. Dig Liver Dis. 2017;49(1):57-62.
9. Tanoglu A, Kara M. Nonalcoholic fatty liver disease-related cardiovascular risk: Is there an association with blood hemoglobin levels? Eur J Gastroenterol Hepatol. 2015;27(10):1126-1129.
10. Alimonti A, Bocca B, Lamazza A, Forte G, Rahimi S, Mattei D, et al. A study on metals content in patients with colorectal polyps. J Toxicol Environ Health A. 2008;71(5):342-7.
11. Hornik P, Milde D, Trenz Z, Stuzka V. Colon tissue concentrations of copper, iron, selenium, and zinc in colorectal carcinoma patients. Chem. Pap. 2006; 60:297–301.
12. Adris N, Chua ACG, Knuiman MW, Divitini ML, Trinder D, Olynyk JK. A prospective cohort examination of haematological parameters in relation to cancer death and incidence: the Busselton Health Study. BMC Cancer. 2018;18(1):863.
13. Lorenzi M, Lorenzi B, Vernillo R. Serum ferritin in colorectal cancer patients and its prognostic evaluation. Int J Biol Markers. 2006;21(4):235-41.
14. Nelson RL. Iron and colorectal cancer risk: human studies. Nutr Rev. 2001;59(5):140-8.
15. Kucharzewski M, Braziewicz J, Majewska U, Gózdz S. Selenium, copper, and zinc concentrations in intestinal cancer tissue and in colon and rectum polyps. Biol Trace Elem Res. 2003;92(1):1-10.
16. Shen C, Shi X, Al-Ashoor M, Xu C. Association between Hemoglobin Levels and Colorectal Polyps in Asymptomatic Chinese Adults. Gastroenterol Res Pract. 2020;2020:3808163.
17. Hashimoto Y, Tanaka M, Kimura T, Kitagawa N, Hamaguchi M, Asano M, et al. Hemoglobin concentration and incident metabolic syndrome: a population-based large-scale cohort study. Endocrine. 2015;50(2):390-6. DOI:10.1007/s12020-015-0587-9.
18. Tal S, Melzer E, Chsherbakov T, Malnick S. Metabolic syndrome is associated with increased prevalence of advanced colorectal polyps. J Nutr Health Aging. 2014;18(1):22-5.
19. Kim BJ, Kim YH, Sinn DH, Kang KJ, Kim JY, Chang DK, et al. Clinical usefulness of glycosylated hemoglobin as a predictor of adenomatous polyps in the colorectum of middle-aged males. Cancer Causes Control. 2010;21(6):939-44.
20. Delavari A, Mardan F, Salimzadeh H, Bishehsari F, Khosravi P, Khanehzad M, et al. Characteristics of colorectal polyps and cancer; a retrospective review of colonoscopy data in Iran. Middle East J Dig Dis. 2014;6(3):144-50.
21. Yang W, Chang Y, Huang H, Wang Y, Yu X. Association between Obesity, Serum Lipids, and Colorectal Polyps in Old Chinese People. Gastroenterol Res Pract. 2013;2013:931084. DOI: 10.1155/2013/931084
22. Sun F, Tan YA, Gao QF, Li SQ, Zhang J, Chen QG, et al. Circulating fibrinogen to pre-albumin ratio is a promising biomarker for diagnosis of colorectal cancer. J Clin Lab Anal. 2019;33(1):e22635.
23. Hartman TJ, Albert PS, Snyder K, Slattery ML, Caan B, Paskett E, et al. The association of calcium and vitamin D with risk of colorectal adenomas. J Nutr. 2005;135(2):252-9.
24. Larsson SC, Bergkvist L, Wolk A. Magnesium intake in relation to risk of colorectal cancer in women. JAMA. 2005;293(1):86-9.

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